Emergency Management of Metabolic Encephalopathies in children

To those residents in the front-line (Emergency room)

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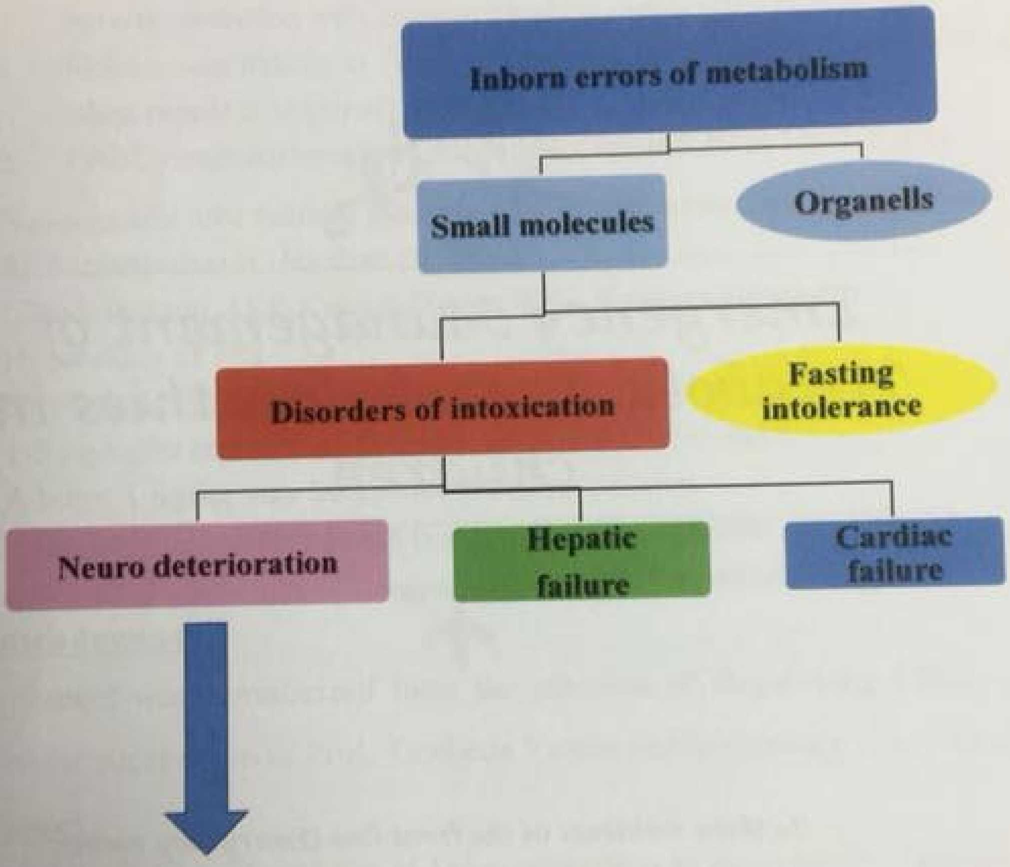
Therapeutic Classifications of Inborn Errors of Metabolism (IEM)



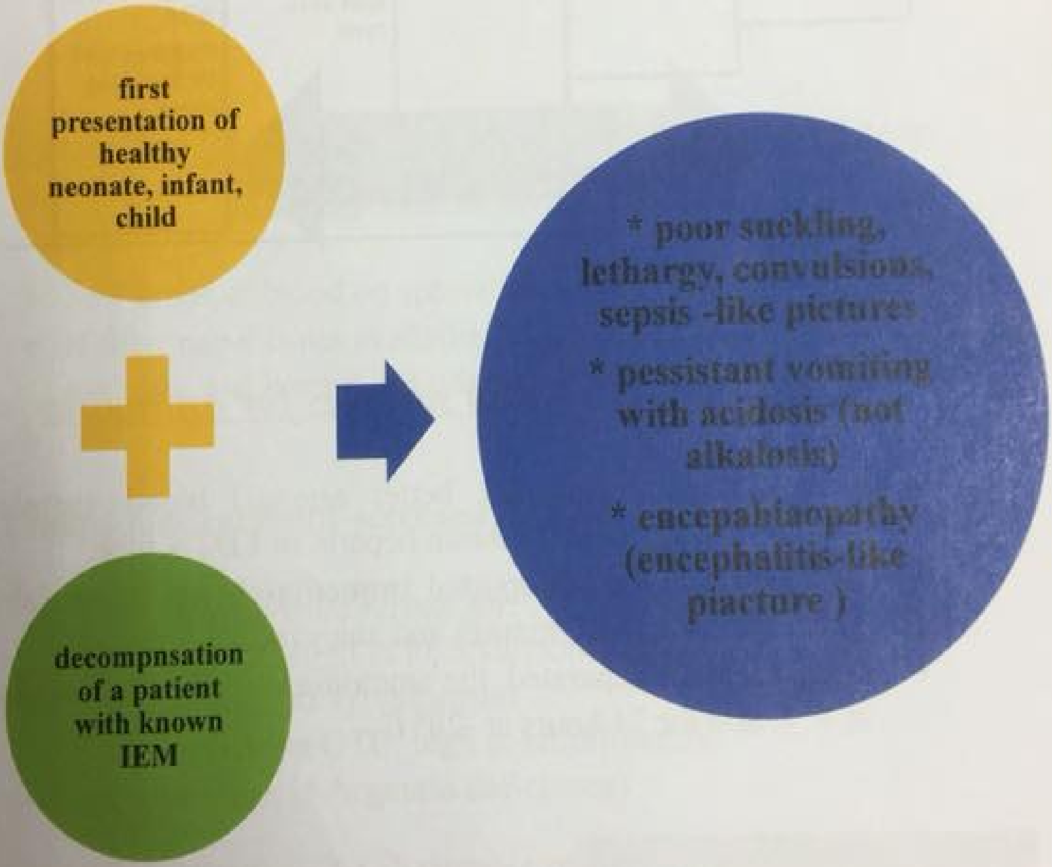
This booklet will include management of this part only

Intoxication is due to:

1. *Exogenous intake* of relatively larger amount of protein than the ability of body to metabolize.
2. *Endogenous* breakdown of protein during episodes of catabolism (stress): infection, surgery, fever.

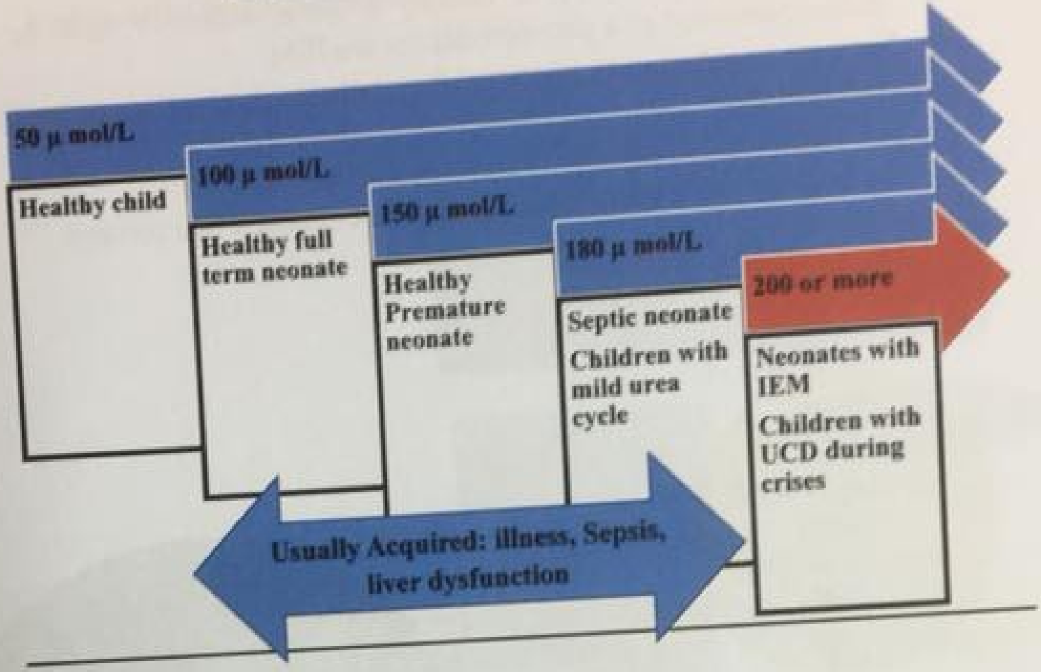
Clinical scenarios

- Either first presentation of healthy neonate, infant or child or a decompensation of a patient with known IEM
- Neonate or infant with poor suckling, lethargy, convulsion or sepsis-like picture
- An infant/ child with persistent vomiting and acidosis
- An infant/child with encephalopathy (encephalitis like picture)


first presentation of healthy neonate, infant, child
decompnsation of a patient with known IEM
* poor suckling, lethargy, convulsions, sepsis -like pictures
* pessistant vomiting with acidosis (not alkalosis)
* encepahlaopathy (encephalitis-like piacture)

If there is any doubt at all, the child must be admitted, even for a short period of observation

Normal ammonia values


50 µ mol/L
Healthy child
100 µ mol/L
Healthy full term neonate
150 µ mol/L
Healthy Premature neonate
180 µ mol/L
Septic neonate
Children with mild urea cycle
200 or more
Neonates with IEM
Children with UCD during crises
Usually Acquired: illness, Sepsis, liver dysfunction

Precautions in taking samples for ammonia

- A free-flowing venous (or better arterial) blood sample should be collected on lithium heparin or EDTA tube.
- Sample should be transported **immediately** on ice to lab. Separated within 15 minutes and analyzed immediately.
- Once plasma is separated, the ammonia is stable for 4 hours at 4° C and for 24 hours at -20° C.

Pitfalls in taking samples for ammonia

- Difficult sampling and hemolysis can cause false increase.
- The ammonia of standing blood increase spontaneously due to: generation and release of ammonia from RBCs and to a lesser extent, from deamination of amino acids by enzymes in circulation

Pitfalls in measuring lactate

- Arterial samples are more reliable
- venous obstruction by tourniquet, crying, or breath holding may increase plasma lactate concentrations by two- to three folds!!!
- Serum lactate can also be increase in hypoxia, infections, convulsions, cardiac disease

Extended Metabolic Screen (EMS) using Tandem Mass Spectrometry (TMS)

- Few drops of blood on special filter paper
- If filter paper is not available, take one ml on heparin (green top) tube and keep it in Fridge (not freezer).

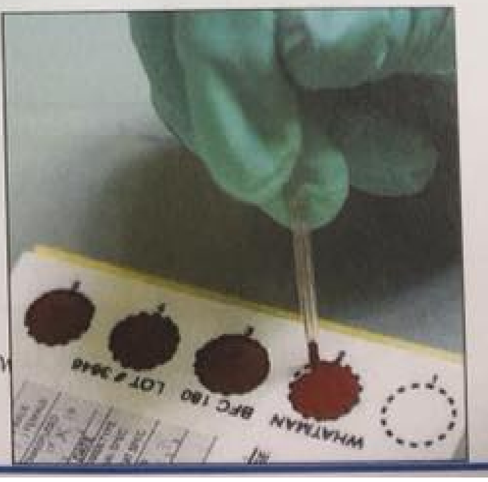
Compounds currently screened by EMS

1- Aminoacids profile screen for:

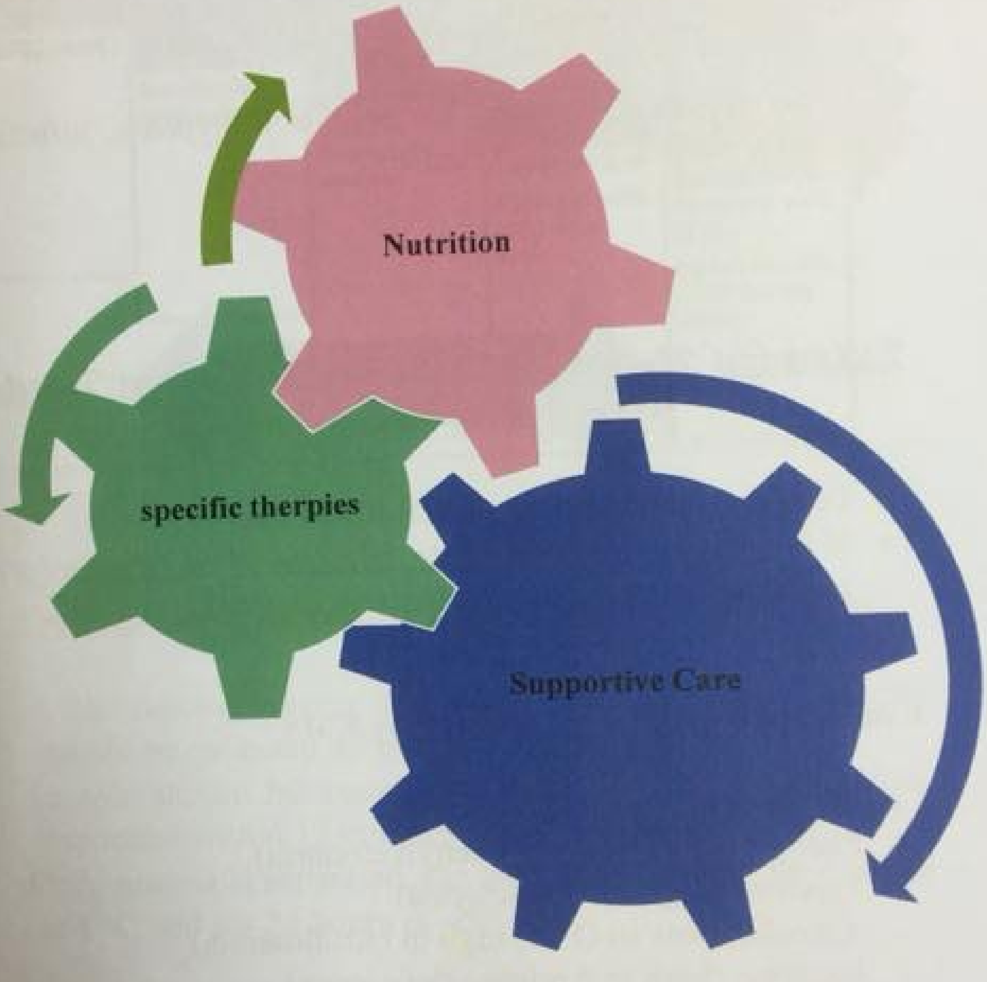
- Phenylalanine (high in Phenylketonuria)
- Tyrosine (high in Tyrosinemia)
- Citrullin (low in OTC, high in citrullinemia)
- Arginine (high in Arginase deficiency)

2- Acylcarnitine profile screen for:

- Fatty acid oxidation defects
- Organic acidemias



Pearls in management of IEM



REMEMBER

Aggressive treatment before the confirmation of a diagnosis may be lifesaving and may reduce the neurological squeals of some of these disorders

1- **Supportive care:**

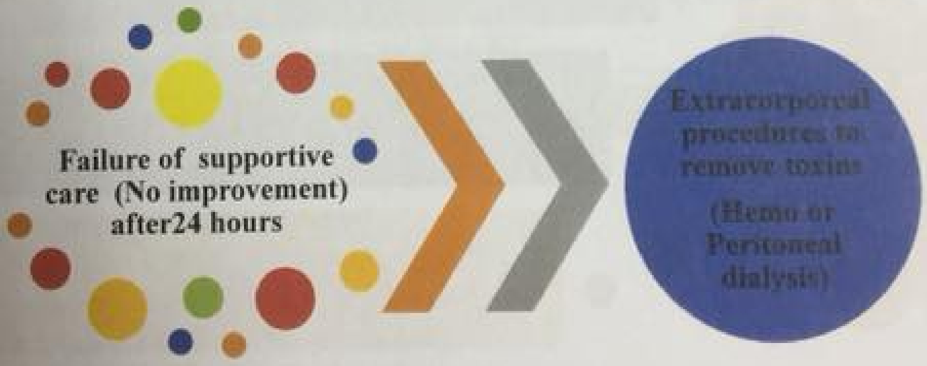
- Most patients will need rehydration, adequate calories, correction of acidosis, electrolytes, calcium, and phosphorus.
- Most patients have functional immunodeficiency which can result in persistent catabolism and therapeutic failure and so infections must be prevented and properly treated.

2- **Nutrition: Extremely important**

- Stop incriminated substance (protein). for not more than 24 hours
- Supply a good source of energy (IV glucose 10%)

3- **Specific therapies:**

- This is used for some disorders and includes substances that enable ammonia excretion (Na benzoate), carnitine, and vitamins (Cofactors).

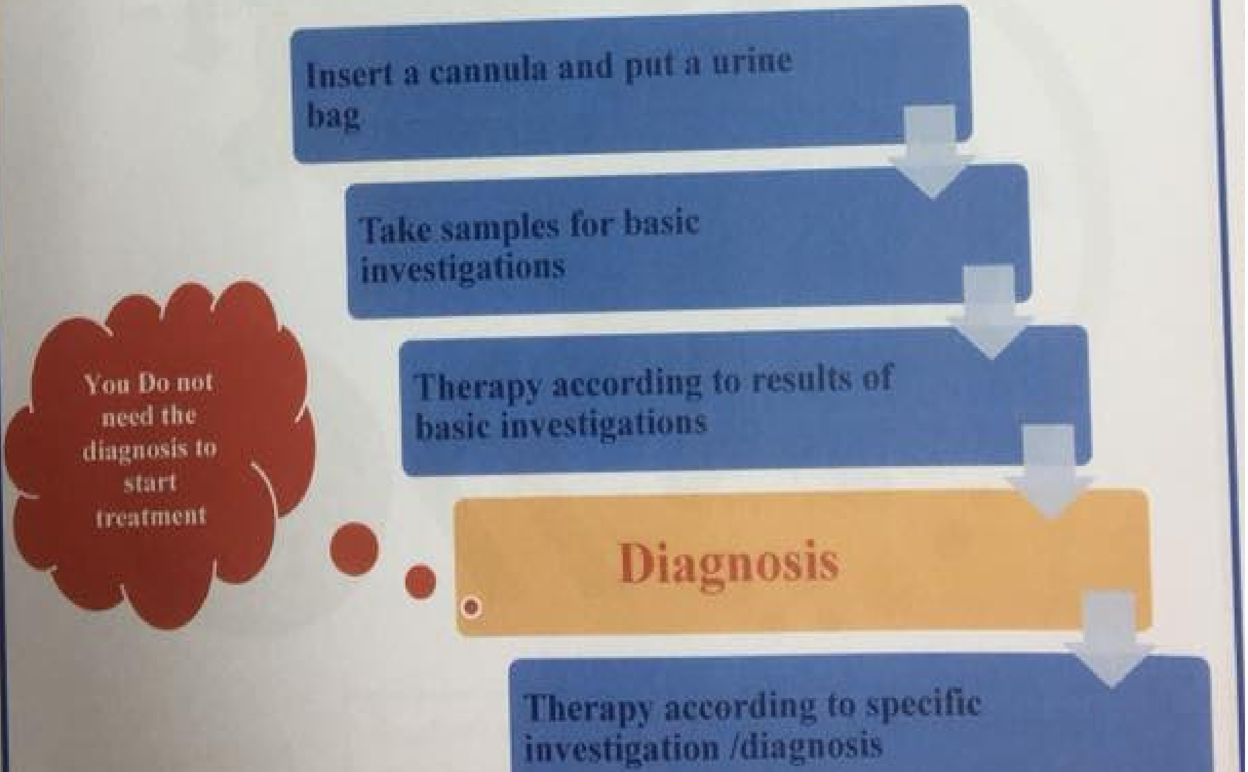

Failure of supportive care (No improvement) after24 hours
Extracorporeal procedures to remove toxins
(Hemo or Peritoneal dialysis)

Emergency Management of UNDIAGNOSED Inborn errors of metabolism

Aims:

1. Stop accumulation of toxic metabolites.
2. Prevention of catabolism (provide adequate calories) to prevent further catabolism
3. Enhance the excretion of toxic metabolites.
4. Co-factor therapy for specific disease and also empirically if diagnosis not established.
5. Symptomatic and Supportive care

Steps



Insert a cannula and put a urine bag

Take samples for basic investigations

Therapy according to results of basic investigations

Diagnosis

Therapy according to specific investigation /diagnosis

You Do not need the diagnosis to start treatment

How to achieve Aims

1- Stop toxic metabolites

- Stop protein intake

2-Prevent further catabolism

- Provide adequate calories by glucose infusion (10%)/ pediament solution. (2 ml/kg over few minutes (then deficit and maintenance pediament solution).

- If hyperglycemia develop , add insulin (0.01-0.1 IU/kg/hr) to enhance anabolism. Monitor very closely and withdraw gradually with normalization of blood glucose

3- Enhance the secretion of toxic metabolites

- L-carnitine (IV or oral) 100 -200 mg/kg/day in 3-4 divided doses

4- Give all cofactors in undiagnosed patient

- Vitamin B1 and B6 : 100 mg/day each (Neurovit or neurobione)
- Vitamin B2 :100mg/day
- Vitamin B12 : Hydroxycobolamine (Depovit 1 mg/day)
- Biotine : Biotine fort: 10 -20 mg /day

5- Symptomatic and supportive care

- Correct dehydration (always needed)
- Correct acidosis if present
- Correct hyperammonemia if present
- Correct hypoglycemia if present
- Give antibiotic (always needed)
- Give anticonvulsants if needed

A Useful check list

1- **Insert an IV access and a urine bag!**	

2- Take samples

A-Basic laboratory investigations

• Blood gases and pH, anion gap (venous)	
• Ammonia	
• Lactate	
• Serum glucose and urine ketones.	
• CBC, CRP	
• Electrolytes (Na, K, Ca, ph, Cl (if available))	
• ALT, AST	
• Creatinine, urea, uric acid	
• Coagulation studies	

B-Specific laboratory investigations:

• Extended (expanded) metabolic screening (blood on filter paper or keep 1 cc blood on a heparinized tube)	
• Urinary organic acids including orotic acid (First voided urine) • keep it in the freezer if the lab is closed	

Do not wait for the urine to start IV fluids

3- Emergency treatment:

Fat should not be given till FAO defects have been excluded

Do not stop IV glucose of hyperglycemia develops. Start insulin 0.01-0.1 units /kg /h with close monitoring

1- **Stop intake** of all potentially toxic compounds (mostly **proteins**) for not more than 24 hours.

2- **Give glucose infusion of a 10% solution** or pediament (2 ml/kg over few minutes. Then correct deficit and give maintenance solution

3- **Give L carnitine** IV or oral at a dose of 200 mg/kg/day in three or four divided doses

4- **Give vitamins** B1, B2, B6 (100 mg/day each or neurovit or neurobione).

5- Also, B12 hydoxycobolamine (Depovit) 1 mg /day IM

6- And biotine 10 mg/day (biotine fort) oral or IV

7- Symptomatic and supportive care:

- **Correction of dehydration**
- **correction of hyperammonemia**
- **correction of metabolic acidosis**
- **Treatment of convulsions**
- **Give antibiotics**

- **Do not stop IV glucose of hyperglycemia develops.**
- **Start insulin at a dose of 0.01- 0.1 units /kg /h with close monitoring**

Treatment of hyperammonemia

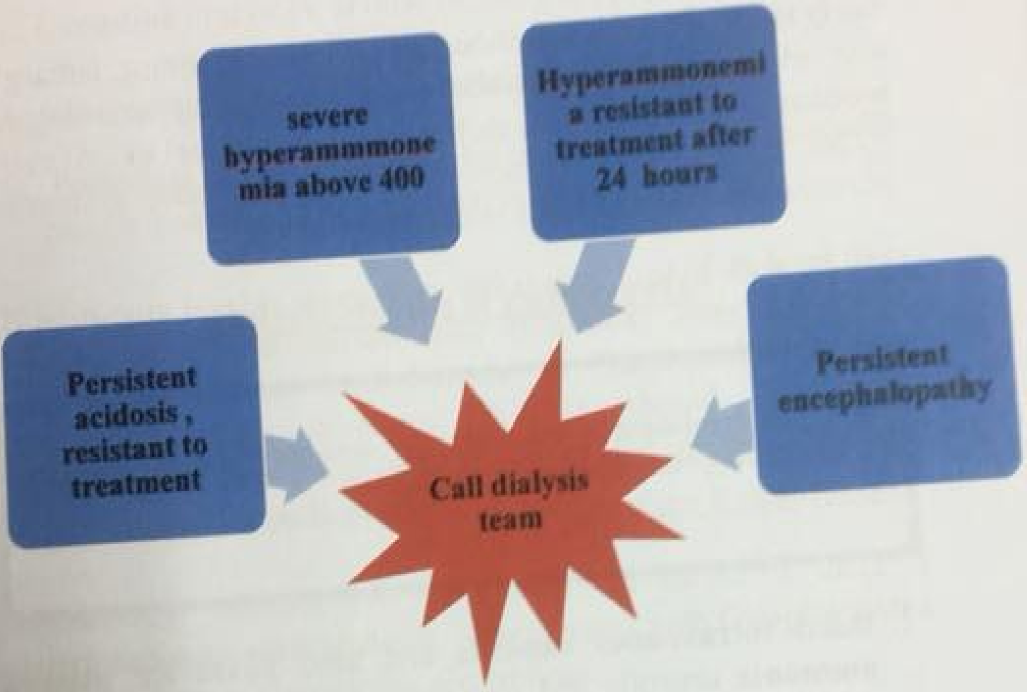
- You have already stopped protein intake
- Give Sodium benzoate or sodium phenylacetate 250 mg / Kg as a primary infusion in a 90 minutes period. Then 250 -500 mg/ Kg/day as a maintenance.
- You can add lactulose and neomycin/flagyl
- If ammonia level is > 400 u mol/ L or if its level does not decrease with conservative treatment in 24 hrs, peritoneal dialysis should be started.
- Entral nutrition (with restrictions) should be started ASAP by continuous entral slow drip feeding via nasogastric tube with minimal amount of protein (0.25 gm / Kg / day) during the first 24 hours of therapy.

Treatment of metabolic acidosis

1- **Correct dehydration**
2- if acidosis persists after correction of dehydration, give sodium bicarbonate if **the pH <7.2** or the **pH is deteriorating rapidly** or the **base deficit is greater than 10 mmol/l.**
3- Give a half correction [0.6 x body weight x base deficit] with sodium bicarbonate **over at least 30 minutes**. And reche
4- Repeat **once** if necessary and keep an eye on plasma **sodium** concentrations. **Aggressive therapy with repeated boluses of IV bicarbonate may induce hypernatraemia, cerebral oedema, and even cerebral haemorrhage.**
5- If no response, and the patient is well hydrated, have no cardiomyopathy or pancreatitis, **CALL for peritoneal dialysis and ventilator support**
6-

Severe acidosis (pH <7.2 or base deficit > 10 mmol/l) **is potentially very dangerous.** Patients may have a respiratory (or cardiac) arrest and are usually difficult to resuscitate. **Always** consider elective assisted ventilation

When to call the dialysis team ???


severe hyperammmonemia above 400
Hyperammonemia resistant to treatment after 24 hours
Persistent acidosis , resistant to treatment
Persistent encephalopathy
Call dialysis team

Impending death and Post mortem samples

- Urine, frozen: organic acids
- Frozen heparinized plasma (Do not use EDTA): aa, carnitine/acylcarnitine profile
- A small snip of skin obtained using sterile technique and stored in tissue culture medium, or sterile saline.
- A liver biopsy (Additional tissue should be preserved for electron microscopy.)

Management of specific diseases

Urea Cycle defect due to OTC deficiency

Decompensation is often triggered by metabolic stress: febrile illness, fasting and any protein loading but sometimes there is no apparent cause.

Early signs of decompensation may be subtle: vomiting, lethargy, loss of appetite or exacerbation of pre-exiting neurological problems (irritability, fits, etc) or just does not feel ok. At early stages the ammonia is not so increased because glutamine accumulates first and leads to cerebral oedema.

Always listen to parents carefully.

Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or is behaving oddly.
Do not delay if you are uncertain.

1. Insert **intravenous cannula** and send blood for **plasma ammonia** urgently and also for urea, electrolytes, glucose, CBC, blood culture.
2. **Stop intake of protein**
3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament)**:** Quickly calculate the deficit and maintenance and prepare the intravenous fluids. If hyperglycemia develops, start insulin as indicated before.
4. Give loading dose of **sodium benzoate** 250 mg/kg (added to glucose over 1-2 hours) then maintenance sodium benzoate 250-500 mg/kg/day.

5. **Arginine** (Note: some parents carry supplies of these): 200-600 mg/kg and maintenance of 100-170 mg/kg/day (some patients may need up to 400-700mg/kg/day)

6. Prevent constipation by giving lactulose

7. **Carnitine** oral or IV at dose of 100 mg/kg/day

8. Give antibiotic and properly treat infection.

9. Potassium should be added once urine flow is normal and the plasma potassium concentration is known.

If ammonia level is more than 400 u mol/ L or if its level does not decrease with conservative treatment after 24 hours, continuous venous hemodialysis or haemoinfiltration or haemodiafiltration, peritoneal dialysis should be started depending on the local availability of the method and the experience of the medical staff.

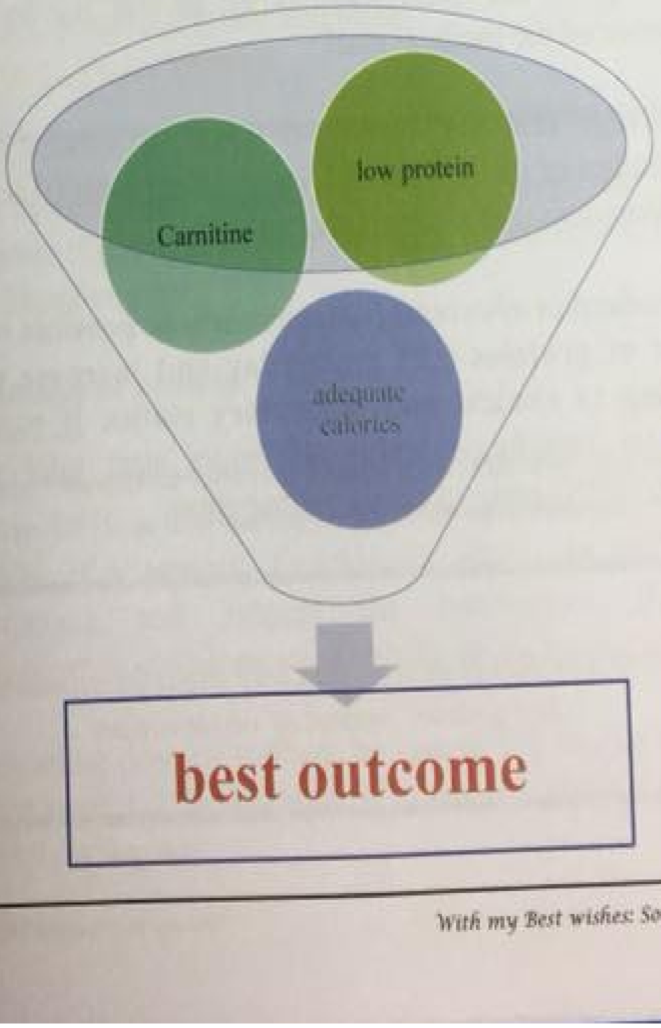
Monitoring: reassess every 4-6 hours or earlier if there is deterioration of clinical status. Assess using both Glasgow coma scale, ammonia, glucose and electrolytes

***Re-introduction of enteral feeds*: as early as possible with small amount of proteins 0.25 gm/kg/day and increase gradually according to clinical and laboratory status.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

If there is any doubt at all, the child must be admitted, even for a short period of observation

Pearls in Emergency Management of Organic acids disorders

For many organic acid disorders, early diagnosis and treatment can significantly change the outcome of the patient. Improved outcome is noted in most cases when the infant is provided ***a low-protein diet and carnitine supplementation****. For some organic acid disorders,* ***additional dietary supplements and/or vitamins are recommended****. Aggressive treatment during metabolic crises, including glucose administration, is recommended.*



Methylmalonic acidemia (MMA)

MMA is caused by a deficiency of methylmalonyl CoA mutase, an enzyme on the catabolic pathway of protein metabolism (methionine, threonine, valine and isoleucine) and cholesterol side chains, odd chain fatty acids and free propionate from the gut. **The co-factor for the enzyme is a derivative of vitamin B_{12} (hydroxocobalamin).**

Decompensation is often triggered by **metabolic stress** such as febrile illness, particularly diarrhoea or vomiting, fasting or constipation, but **an obvious precipitant cause is not always apparent.** Early signs of decompensation may be subtle: lethargy, decreased appetite, irritability or just "does not look ok". Vomiting is common and should always be taken seriously.

Please always listen to parents carefully

- **Dehydration** is a common problem because of the renal disease and polyuria.
- **Emergency treatment should be meticulous as there is a high risk of serious complications like encephalopathy, stroke like episode, metabolic acidosis, pancreatitis and cardiomyopathy.**
- **Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.**

In MMA, the maintenance fluid is calculated as follows (because of increased fluids requirements: **120ml/kg for 1st 10 kg then 60 ml/kg for next 10 then 25ml/kg).**

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH, blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine, amylase. calcium, phosphorus and alkaline phosphatase.**

2. **Stop protein intake (for not more than 48 hours)**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg over few minutes until the maintenance solution is ready (Pediament)**:** Quickly calculate the deficit and maintenance and prepare the intravenous fluids. **Insulin may be added as indicated before**

4. **Give L- Carnitine** oral or IV at dose of 200 mg/kg/day in 3-4 doses. (some references advise a loading dose of 100 mg/kg over 30 minutes followed by a continuous infusion of 4mg/kg/hour as a maintenance)

5. **Correct metabolic acidosis** as described before.

6. **Correct hyperammonemia as described before.**

7. Give **Metronidazole** 7.5 mg/kg per dose 8 hourly

8. If the patient is vitamin B_{12} responsive or B_{12} status is not known, give **hydroxocobalamin 1 mg intramuscularly**

9. Treat any **infection with proper antibiotics**

10. Treat **constipation** (which increases propionate absorption from the gut).

11. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominal ultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

Cardiomyopathy may develop for no reason at any time. If you suspect cardiomyopathy arrange for Echocardiography and call for cardiologist.

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose, lactate, urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

Medicines to be avoided - Sodium Valproate

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Propionic acidemia

It is one of the protein IEM caused by a deficiency on propionyl CoA carboxylase, an enzyme on the catabolic pathway of aminoacids (isoleucine, valine, threonine and methionine) as well as cholesterol side chains, odd chain fatty acids and free propionate from the gut.

Decompensation is often triggered by metabolic stress such as febrile illness, particularly diarrhoea or vomiting, fasting, or constipation. Decompensation may be manifested by lethargy, refusal of eating, irritability or just 'not right'.

- **Please, always listen to parents carefully.**

- **Emergency treatment should be meticulous as there is a high risk of serious complications like encephalopathy, stroke like episode, metabolic acidosis, pancreatitis and cardiomyopathy.**
- **Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.**

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH and blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine, amylase. calcium, phosphorus and alkaline phosphatase.**
2. **Stop protein (for not more than 48 hours).**
3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids

4. **Correct metabolic acidosis** as described before
5. **Correct hyperammonemia** as described before
6. **Give Carnitine** oral or IV at dose of 100 – 200 mg/kg/day
7. Give **Metronidazole** 7.5 mg/kg per dose 8 hourly
8. Treat any **infection with proper antibiotics**
9. Treat **constipation** (which increases propionate absorption from the gut). Do **not** use lactulose as this can be fermented to propionate by gut bacteria)
10. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominalultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

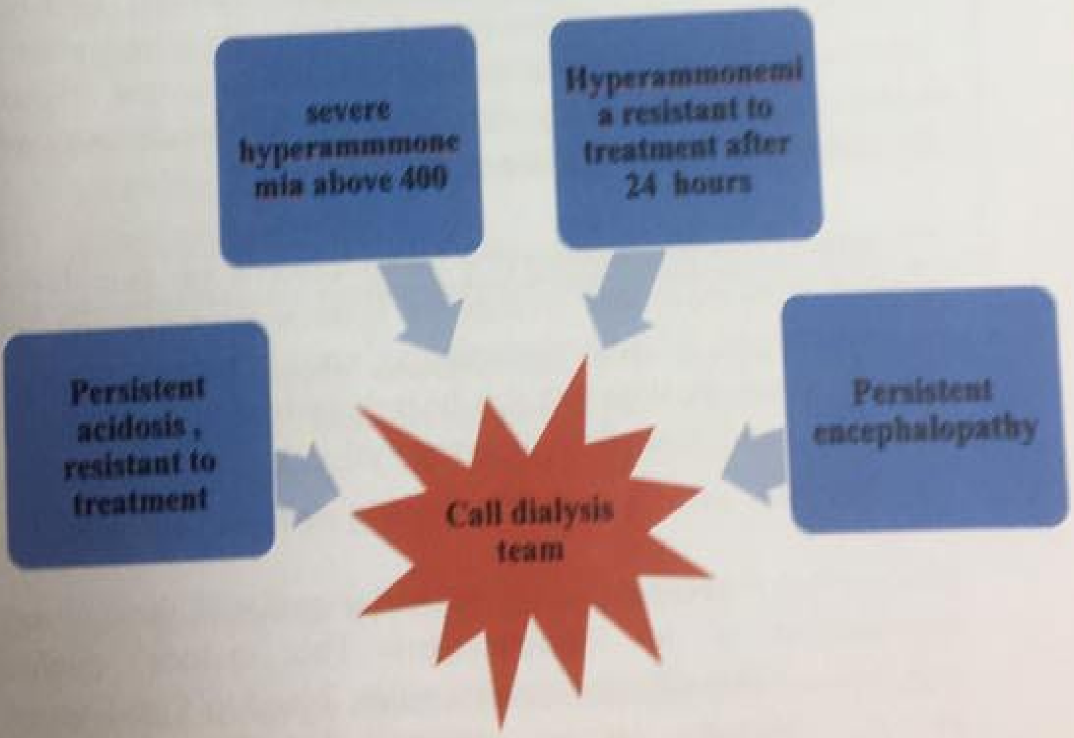
*****Cardiomyopathy*** may develop for no reason at any time. If you suspect cardiomyopathy arrange for Echocardiography and call for cardiologist. Cardiac arrhythmias, notably long Q-T, are an important complication that may be responsible for sudden death. These may vary from time to time so all sick patients should be on a monitor.

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose , lactate , urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

Medicines to be avoided - Sodium Valproate; Lactulose.

If there is any doubt at all, the child must be admitted, even if only necessary for a short period of observation.


severe hyperammmonemia above 400
Hyperammonemia a resistant to treatment after 24 hours
Persistent acidosis , resistant to treatment
Persistent encephalopathy
Call dialysis team

Isovaleric acidemia

Isovaleric acidaemia is caused by a deficiency of isovaleryl CoA dehydrogenase, **an enzyme on the catabolic pathway of leucine**. Treatment is aimed at reducing production of isovaleric and increasing its removal. **The patients are treated with a low protein diet, glycine and carnitine**

Decompensation is often triggered by metabolic stress such as febrile illness, particularly diarrhoea or vomiting, fasting, or constipation. Decompensation may be manifested by lethargy, refusal of eating, irritability or just 'not ok'.

Please, always listen to parents carefully.

Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain. There is high incidence of pancreatitis

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH and blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine and amylase, calcium, phosphorus, alkaline phosphatase**
2. **Stop protein (for not more than 48 hours).**
3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament)**:** Quickly calculate the deficit and maintenance and prepare the intravenous fluids
4. **Correct metabolic acidosis** as described before
5. **Correct hyperammonemia** as described before

6. **Give Carnitine** oral or IV at dose of 100 – 200 mg/kg/day
7. Give **Glycine** via nasogastric tube at a dose of 300 mg/kg per day.
8. Treat any **infection with proper antibiotics**
9. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominal ultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose, lactate , urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

If there is any doubt at all, the child must be admitted, even if only necessary for a short period of observation.

Maple syrup Urine disease (MSUD)

MSUD is disorder affecting the breakdown of branched chain amino acids (BCAA: Leucine, Isoleucine & Valine). Encephalopathy in decompensated patients is the result of accumulation of the BCAA (particularly leucine), which are toxic at high concentrations. **There may be NO hypoglycemia, hyperammonaemia or acidosis**.

Decompensation: often triggered by metabolic stress such as febrile illness, particularly gastroenteritis or fasting but **an obvious cause is not always apparent.**

Early signs: lethargy, irritability or just 'not right'. **vomiting is common and should always be taken seriously.**

Please Always Listen to parents carefully

Treatment aims: at a point you may need individual aminoacids

- *Inhibit protein catabolism and promoting anabolism* by providing **high calorie intake** combined with the **child's usual MSUD amino acid formula.**
- *Lower BCAA levels* by **stopping or restricting 'natural protein.**
- Ensure *a balance is maintained between leucine, isoleucine and valine* during decompensation giving **supplements of individual aminoacids.**

1. Insert **intravenous cannula** and send blood for **plasma aminoacids or EMS (whatever available) , pH and blood gases, CBC and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine and amylase.**

2. **Stop protein intake**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids **Hyperglycaemia can be a problem. If hyperglycemia developed start an insulin as indicated before.**

4. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

5. Intra-lipid may be added 2g/kg/d (0.4ml/kg/hour of 20% solution).

6. Treat any infection properly

7. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

Monitoring: Reassess after 4-6 hours or earlier if there is any deterioration or no improvement call for peritoneal dialysis (although less efficient than hemodialysis).

Re-introduction of enteral feeds: enteral feeds should be used as early as possible to promote anabolism and protein synthesis.

The BCAA free aminoacid mixture should be given as tolerated and natural protein introduced adjusted according to the plasma BCAA concentrations. The branch chain aminoacid free aminoacid mixture should be added starting with a low dose 0.5 g /kg/d. This should be increased as quickly possible to 2 g/kg/d.

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Fatty Acid Oxidation defects (FAO)

Please Always listen to parents carefully

- **Hypoglycaemia only occurs at a relatively late stage (or very late) so Do not delay treatment just because the blood glucose is not low.**
- **The aim should always be to intervene whilst the blood glucose is normal.**

- ***Decompensation*** is often triggered by metabolic stress such as febrile illness, infections, fasting and particularly vomiting and diarrhea can lead to serious illness with encephalopathy and hypoglycaemia. The early signs of decompensation may be subtle **(lethargy or 'floppiness)**.

The major complications are **encephalopathy, cardiomyopathy, hypoglycaemia and rhabdomyolysis.**

Treatment aims:

1. To restore carnitine concentrations
2. Reduce mobilization of fat by providing ample glucose - enteral or intravenously.

Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.

1. Insert **intravenous cannula** and send blood pH and blood gases Glucose (laboratory and bedside strip) CBC, creatinine, electrolytes.
2. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids
3. **Give Carnitine** IV at dose of 100-200 mg/kg/day, oral if IV carnitine is not available
4. Treat any **infection with proper antibiotics**
5. Treat metabolic acidosis if present

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment with Glasgow coma score, Blood pH and gases , Glucose , Urea and electrolytes.

Restart oral feeds as soon as possible; once the child is has stopped vomiting.

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Rhabdomyolysis, myoglobulinuria

- The early signs may be subtle **(weakness, lethargy or 'floppiness)**

Please Always listen to parents carefully

Emergency treatment should be meticulous as there is a high risk of serious complications including:

- Leakage of myoglobin into the systemic circulation, with a risk of **renal vasoconstriction and acute renal failure**
- The leakage of potassium into the systemic circulation, with potentially life-threatening **acute hyperkalaemia**
- **hyperuricaemia** due to release of purines from disintegrating cell nuclei
- **Hyperphosphataemia** may be due to efflux from damaged muscle cells with potential metastatic calcification and **hypocalciemia**
- **Metabolic acidosis** and aciduria

Start treatment immediately with the first sign of weakness and lethargy. **Do not delay if you are uncertain**. **DO NOT wait till you see the colour of urine.**

1. Insert **intravenous cannula** and **send samples for** CPK, urine myoglobin, potassium, calcium and phosphorus, acid-base status, uric acid, urea and creatinine measurements.

2. Maintenance **of adequate preload and urine output**

3. Maintenance **fluid at 2 – 3 x normal requirements**.

4. **Alkalinisation of urine,** (sodium bicarbonate 1 – 3 mmol/kg/day (IV or orally depending on the clinical status of the patient), given as doses every 4 – 8 hrs) to protect against myoglobin-induced renal failure. **Aim to keep urinary pH above 6.5.** If metabolic alkalosis develops (pH > 7.45) there is a theoretical risk of enhancing metastatic calcification

5. Haemodialysis may be necessary for acute renal failure.

6. Treat any **infection with proper antibiotics**

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment , urine output, Blood and urine pH Urea, creatinine, uric acid, ca, phosphorus, K and **CPK**

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Glutaric aciduria type I (GA type I)

GA type I is a rare inborn error of protein metabolism due to glutaryl-CoA dehydrogenase deficiency which is involved in processing lysine, hydroxylysine, and tryptophan metabolism. Excessive levels of these amino acids and their intermediate breakdown products cause damage to the brain, particularly the basal ganglia.

The **characteristic neurological sequela** is secondary dystonia, superimposed on axial hypotonia.

Emergency treatment should start without delay and should be performed aggressively during febrile illness Gastroenteritis, poor food intake, surgery

1. Insert **intravenous cannula** and send blood for **pH and blood gases, CBC, electrolytes and blood culture.**
2. Stop intake of natural proteins (not more than 24 hours) and then gradually introduce it. Prolongation of inadequately low protein intake increases the risk of protein catabolism.
3. Give high dose IV glucose (2 ml/kg of 10% glucose or pediament) until the maintenance solution is ready (Pediament)**:** Quickly calculate the deficit and maintenance and prepare the intravenous fluids. If hyperglycemia develop add insulin as previously indicated.
4. **Double the dose of L-carnitine** to 200 mg/kg/day
5. Correct the metabolic decompensation as metabolic acidosis, electrolytes, and ammonia

6. Increase caloric intake by frequent carbohydrate feeds especially liquids if tolerated. If lysine free aminoacid mixture available and can be tolerated orally or via naso-gastric tube start with 0.5 g/kg/d but for as short a period as possible. **Do not delay giving other treatment if the mixture is not immediately available.**

7. If body temperature raises above 38.5 °C, antipyretics, such as ibuprofen or paracetamol (each 10-15 mg/kg per single dose, 3-4 doses daily, maximum daily dose 60 mg/kg body weight) should be administered.

8. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment with Glasgow coma score, Blood pH and gases , Glucose , Urea and electrolytes.

Re-introduction of enteral feeds: enteral feeds should be used as early as possible to promote anabolism and protein synthesis

Valpoaric acid and Vigabrtin are CONTRAINDICATED

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.